IMMOBILIZATION STRESS IS ASSOCIATED WITH INCREASED RELEASE OF CRF & BOMBESIN-LIKE PEPTIDES AT THE CENTRAL NUCLEUS OF THE AMYGDALA. J. McIntosh, Z. Merali. School of Psychology and Dept. of Pharmacology, University of Ottawa, Canada.

It is becoming increasingly evident that the amygdala, particularly the central nucleus (Ce), plays a key role in the emotional response to fearful/stressful stimuli. Neurons in the Ce are known to contain both bombesin (BN) and corticotrophin releasing factor (CRF). CRF is believed to mediate the stress induced coincident activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system. However, underlying mechanisms causing CRF release are yet to be fully elucidated. Recent research in our lab has shown that acute stress increased BN-like immunoreactivity and that central administration of BN produces stress-like endocrine changes. Furthermore, pretreatment with a CRF receptor antagonist blocks the endocrine as well as some of the behavioral effects of BN. These results suggest that 1) BN-like peptides play a role in the mediation of the stress response and 2) that this response may be mediated through CRF release. The objective of the current study was to measure endogenous changes in release of BN and CRF in response to acute restraint stress in awake and freely moving animals using *in vivo* microdialysis. Probes were implanted at the Ce and four 30 min baseline samples were collected. Animals were then manually restrained for 20 min. Blood was drawn before and after restraint for ACTH and corticosterone levels. Perfusate samples were then collected every 30 min for up to 3 h. Animals were then exposed to a second session of restraint stress. Blood was again drawn and perfusate sampling continued for an additional 2.5 h. Results revealed a stress-related increase in both BN- and CRF-like immunoreactivity at the Ce. Following the first stress, there was an immediate increase in CRF which declined during the 2nd and 3rd samples. The second stressor produced an even greater rise in the CRF release. BN levels started to rise on the 2nd sample after the first stress, and continued to rise. This response was further enhanced by the 2nd stressor. These results appeared to be specific to the Ce as reflected by the lack of stress-induced changes at non-central amygdaloid sites. Plasma ACTH and corticosterone levels were significantly elevated following both periods of stress; however, this response was attenuated during the second stress suggesting habituation. These results demonstrate a stress related release of both CRH and BN-like peptides at the Ce of the amygdala which increases even more upon expose to a second stressful event. Unlike the stress-induced endocrine changes, these effects are more sustained and less prone to rapid adaptation. It is thus likely that these amygdaloid changes, particularly in the BN release, may mediate the more long-term effects of stress.